ASIA PACIFIC JOURNAL of MEDICAL TOXICOLOGY
APJMT 4;1 http://apjmt.mums.ac.ir March 2015

CASE REPORT

Ethylene Glycol Poisoning; an Unusual Cause of Hyperglycemia: A Case Report

ABDUL RAOOF KUNNUMMAL MADATHODI*, MEKKATTUKUNNEL A. ANDREWS, INDIRA MADHAVAN

Department of Medicine, Government Medical College, Thrissur, Kerala, India

Abstract

Background: Poisoning with ethylene glycol (EG) can be fatal even if appropriate treatments are delivered. EG poisoning usually causes central nervous system depression, cardiovascular dysfunction, metabolic acidosis and acute renal failure (ARF).
Case Report: A 33-year-old man was referred to the emergency department with reduced consciousness and dyspnea of four-hour duration due to unknown reason. The patient had no history of diabetes, hypertension, cardiac disease or asthma. He was tachycardic, tachypneic and hypertensive. Laboratory investigations revealed hyperglycemia, high serum creatinine, hyponatremia, hyperkalemia, leukocytosis and high anion gap metabolic acidosis (HAGMA). He was initially managed as diabetic ketoacidosis (DKA). Alternative diagnoses of toxic alcohols poisoning was considered as there was no improvement. EG ingestion was confirmed when the relatives found an empty bottle of automotive brake oil, a poly glycol-based product, in the patient's room. Although he was treated with ethanol and hemodialysis, renal failure worsened and finally he succumbed to death due to severe sepsis on the seventh day of EG ingestion.
Discussion: This case illustrates the difficulties posed by high toxicity as well as unraveled and delayed diagnosis of EG poisoning. High anion gap and high osmolal gap are characteristics of EG poisoning. Transient pancreatitis caused by EG and insulin resistance due to ARF are the possible explanations for hyperglycemia secondary to EG poisoning.
Conclusion: EG poisoning may manifest with hyperglycemia and HAGMA resembling DKA. It is important for the clinician to have high degree of suspicion for EG poisoning in case of HAGMA and ARF refractory to common treatments.

Keywords: Acidosis; Ethylene Glycol, Hyperglycemia, Poisoning; Renal Insufficiency

How to cite this article: Kunnummal Madathodi AR, Andrews MA, Madhavan I. Ethylene Glycol Poisoning; an Unusual Cause of Hyperglycemia: A Case Report. Asia Pac J Med Toxicol 2015;4:55-7.

INTRODUCTION

Poisoning with ethylene glycol (EG), an extremely toxic alcohol, can be fatal even if appropriate treatments are delivered (1). Intentional ingestion of toxic glycols is not a common method for suicidal attempt in India while unintentional poisoning sometimes happens in children (2).

Absorption of EG through the gastrointestinal tract is rapid (3). Similar to ethanol and methanol, EG is metabolized by the alcohol dehydrogenase to glycolaldehyde and the action by this enzyme is the rate limiting metabolic step for EG (4). Aldehyde dehydrogenase converts EG to glycolic acid and subsequently to oxalic acid. Severe metabolic acidosis with high anion gap is mainly caused by glycolic acid. Oxalic acid precipitates in the form of calcium salt in the renal tubules leading to acute renal failure (ARF) (5).

EG poisoning causes central nervous system (CNS) depression, which can occur within 12 hours leading to coma, as well as cardiovascular system involvement after 12 to 24 hours of ingestion, which induces tachycardia and hypertension (6,7). Hypocalcemia due to oxalate chelation may lead to arrhythmias, tetany and convulsions. ARF ensues after 24 to 48 hours of EG ingestion. Envelope-shaped crystals of calcium oxalate may be seen in the urine except in case of significant renal failure (8). Blood glucose imbalances are relatively uncommon findings following EG poisoning.

In this report, a case of EG poisoning is presented who had reduced consciousness, metabolic acidosis and hyperglycemia at the time of presentation to emergency department which posed diagnostic difficulty as history of poisoning was not evident in the first approach.

CASE REPORT

A 33-year-old man was referred to the emergency department of Government Medical College hospital, Thrissur with reduced consciousness and dyspnea of four-hour duration due to unknown reason. The patient had no history of diabetes, hypertension, cardiac disease or asthma. On examination, he was tachycardic (124 beats/minute), tachypneic (36 breaths/minute) and hypertensive (184/100 mmHg). His chest was clear to auscultation bilaterally.

Baseline laboratory findings showed blood sugar of 488 mg/dL, serum creatinine of 3.6 mg/dL, serum sodium of 128 mEq/L, serum potassium of 7 mEq/L, urine test positive for

*Correspondence to: Abdul Raoof Kunnummal Madathodi; MD. Junior Resident, Department of Medicine, Government Medical College, Thrissur, Kerala, 680561 India.
E-mail: abuihsan437@gmail.com, Tel: + 91 90 4860 9851
Received 16 December 2014; Accepted 21 February 2015

sugar and negative for ketone body, hemoglobin of 17.1 g/dL, leucocyte count of 43,600/mm^3 and platelet count of 380,000/mm^3. Arterial blood gas analysis showed severe metabolic acidosis with pH of 6.89, bicarbonate level of 13 mEq/L and $PaCO_2$ of 33 mmHg.

As patient had hyperglycemia with increased anion gap acidosis the possibility of diabetic ketoacidosis (DKA) was considered, and standard treatments including fluid therapy and insulin infusion were started. Blood sugar returned to less than 200 mg/dL on the second day of admission, but acidosis persisted. At that time, other possibilities of high anion gap metabolic acidosis (HAGMA) with renal failure like methanol poisoning and renal failure were taken into account. Later, patient's relatives could find an empty bottle of DOT3, an automotive brake oil, in the patient's room which was considered as having a relationship with his condition. The product is mainly composed of polyethylene glycols and glycol ethers.

In order to correct the severe acidosis, sodium bicarbonate (150 mEq diluted in 1 L of 5% dextrose) was infused in one hour. As fomepizole was not available, ethanol was given through Ryle's tube. Patient was also given parenteral thiamine and pyridoxine. Due to persistent metabolic acidosis and anuria, emergency hemodialysis was considered for the patient. His mental status improved after hemodialysis and then he confirmed deliberate ingestion of the brake oil.

On the second day evening, the patient complained of blurred vision with difficulty in finger counting. Optic fundi examination revealed bilateral disc edema suggestive of optic neuritis. On the subsequent days, renal function worsened which resulted in blood urea nitrogen (BUN) of 94 mg/dL and serum creatinine of 4.6 mg/dL on third day and BUN of 137 mg/dL and serum creatinine of 9.8 mg/dL and serum potassium of 6.4 mEq/Lon the 5th day. The patient became stuporous on the 3rd day and remained anuric. Moreover, assisted ventilation became necessary and so the patient was intubated. His condition deteriorated on the subsequent days when features of pneumonia emerged on the 5th day and subsequently sepsis occurred. On the 7th day post-ingestion of the poison, the patient died due to uncontrollable sepsis and renal failure. Autopsy revealed total necrosis of both kidneys.

DISCUSSION

This case illustrates the difficulties posed by high toxicity as well as unraveled and delayed diagnosis of EG (and other toxic glycols) poisoning. HAGMA and hyperglycemia at presentation was presumed to be due to DKA, while other differential diagnoses related to co-occurrence of these clinical features can be chronic renal failure, multiple organ failure, and critical illness (7). Alcoholic ketoacidosis caused by excessive alcohol use in a malnourished person, methanol poisoning and EG poisoning are also responsible for HAGMA (9).

The mortality of EG poisoning varies from 1 to 22% (5,9). The highest mortality is found in patients with severe metabolic acidosis (blood pH < 7.1) or initiation of treatment later than 10 hours after exposure, which both situations were present for our patient. The lethal dose of EG has been reported to be 1.4 to 1.5 mL/kg body weight, although death has been reported with lower amounts, and survival has been reported with much greater amounts (6,7).

Common clinical features of EG poisoning comprises of neurologic abnormalities such as CNS depression, cardiopulmonary dysfunction and renal failure which occasionally can be present simultaneously in a patient. Rarely, ARF can be seen in the absence of other clinical and laboratory features of EG poisoning and so this entity should be considered in the differential diagnoses of unexplained ARF (7). High anion gap and high osmolal gap are characteristics of EG poisoning. Serum osmolality increases after few hours of EG ingestion, later decreases as EG is metabolized, but osmolal gap remains high. Apart from presence in the urine, calcium oxalate crystals can be deposited in kidneys, brain, lungs and myocardium and may be the only evidence of EG ingestion in some patients with normal anion and osmolal gap (7). The distinct characteristic of our patient compared to other reported cases of EG poisoning was hyperglycemia. Thrall et al reported hyperglycemia in dogs and cats poisoned with EG (10). In addition, Ybarra et al found DKA in 5 patients poisoned with EG, who 4 of them were previously diabetic and one of them had no history of diabetes (11). Except these two articles, no similar reports on EG poisoning with hyperglycemia could be found in the available literature. As can be seen, high blood sugar is a rare condition in EG poisoning which confuses the clinician with DKA, and so the patient would not recover until detoxification treatments such as fomepizole (or ethanol) and early hemodialysis are given. Two possible explanations can be suggested for the hyperglycemia secondary to EG poisoning. First of all, EG poisoning is known for causing transient pancreatitis which results in reduction of serum insulin level (9,11). Second, insulin resistance can be seen in association with ARF (12), and our patient developed refractory ARF.

Moreover, our patient developed impaired vision in the initial days of admission which can be explained by the fact that DOT3 compounds contain some amounts of methyl alcohol. Hyperglycemia following methanol poisoning has also been reported in the literature so far (9). It should be noted that this type of compound(DOT3) are also formed from diethylene glycol (DEG) which can cause similar clinical features to EG, though calcium oxalate crystals that are typical of EG toxicity may not be found after DEG poisoning (9,13). What is more, pancreatitis is more common after DEG poisoning (9).

It is crucial for emergency physicians, to consider the possibility of methanol or EG poisoning in patients with reduced consciousness and HAGMA. However, the measurement of serum methanol and EG concentrations is usually performed by gas chromatography which is not available in all medical settings. Patient management for EG poisoning includes correction of metabolic acidosis and prevention of calcium oxalate precipitation. Activated charcoal and nasogastric lavage have minor role in the management, as EG is rapidly absorbed from the gastrointestinal tract. Endotracheal tube may be placed to protect the airway when patient is in coma (1,14). The affinity of alcohol dehydrogenase is more to ethanol than EG and so

the ethanol can be used as antidote. Fomepizole is a safer and more effective alternative (1), but it is more expensive and usually not available in most settings especially in developing countries. Hemodialysis should be rapidly taken into account for persistent metabolic acidosis concurrent with renal failure (14-16). Diuresis has been found to be impractical because alcohols cannot be concentrated in the urine. Hemodialysis, can clear the body from the poison at rates of at least 60% of the blood flow rate through the coil (17,18). Hence, patients with EG ingestion are better to be loaded with fomepizole or ethanol and transferred to a hemodialysis setting. Pyridoxine and thiamine are cofactors in EG metabolism and some scientists advocate the parenteral use of these agents (9,14).

CONCLUSION

EG poisoning may manifest with hyperglycemia and HAGMA resembling DKA. It is important for the clinician to have high degree of suspicion for EG poisoning in case of HAGMA and ARF refractory to common treatments.

ACKNOWLEDGEMENT

We thank all staff members of department of medicine, Government Medical College, Thrissur, India.

Conflict of interest: None to be declared.

REFERENCES

1. Brent J. Current management of ethylene glycol poisoning. Drugs 2001; 61:979-88.
2. Singh J, Dutta AK, Khare S, Dubey NK, Harit AK, Jain NK, et al. Diethylene glycol poisoning in Gurgaon, India, 1998. Bull World Health Organ 2001;79:88-95.
3. Stinson RA. Ethylene glycol poisoning. Lancet 1985;2:552.
4. Sullivan JB, Krieger GR. Clinical Environmental Health and Toxic Exposures. 2nd ed. Philadelphia, USA: Lippincott Williams & Wilkins; 2001.
5. Porter WH. Ethylene glycol poisoning: quintessential clinical toxicology; analytical conundrum. Clin Chim Acta 2012;413:365-77.
6. Karlson-Stiber C, Persson H. Ethylene glycol poisoning: experiences from an epidemic in Sweden. J Toxicol Clin Toxicol 1992;30:565-74.
7. Eder AF, McGrath CM, Dowdy YG, Tomaszewski JE, Rosenberg FM, Wilson RB, et al. Ethylene glycol poisoning: Toxicokinetic and analytical factors affecting laboratory diagnosis. Clin Chem 1998;44:168-77.
8. Spillane L, Roberts JR, Meyer AE. Multiple cranial nerve deficits after ethylene glycol poisoning. Ann Emerg Med 1991;20:208-10.
9. Kraut JA, Kurtz I. Toxic alcohol ingestions: clinical features, diagnosis, and management. Clin J Am Soc Nephrol 2008;3:208-25.
10. Thrall MA, Grauer GF, Mero KN. Clinicopathologic findings in dogs and cats with ethylene glycol intoxication. J Am Vet Med Assoc 1984;184:37-41.
11. Ybarra J, Doñate T, Pou JM, Madhun ZT. Ethylene Glycol intoxication with and without simultaneous diabetic ketoacidosis: A report of nine cases and review of the literature. Int J Diabetes Metab 2005;13:83-7.
12. Mehta RL. Glycemic control and critical illness: is the kidney involved? J Am Soc Nephrol 2007;18:2623-7
13. Schep LJ, Slaughter RJ, Temple WA, Beasley G. Diethylene glycol poisoning. Clin Toxicol (Phila) 2009;47:525-35.
14. Barceloux DG, Krenzelok EP, Olson K, Watson W. American Academy of Clinical Toxicology Practice Guidelines on the Treatment of Ethylene Glycol Poisoning. Ad Hoc Committee. J Toxicol Clin Toxicol 1999;37:537-60.
15. Jacobsen D, Ovrebo S, Ostborg J, Sejersted OM. Glycolate causes the acidosis in ethylene glycol poisoning and is effectively removed by hemodialysis. Acta Med Scand 1984;216:409-16.
16. Sharma N, Jain S. Toxicity of brake oil. Emerg Med J 2002;19:267-8.
17. Tanasescu A, Macovei RA, Tudosie MS. Outcome of patients in acute poisoning with ethylene glycol--factors which may have influence on evolution. J Med Life 2014;3:81-6.
18. Bobbitt WH, Williams RM, Freed CR. Severe ethylene glycol intoxication with multisystem failure. West J Med 1986;144:225-8.